(b) contacting said polypeptide or fragment with said compound; and

(c) determining whether the activity of said polypeptide or fragment is modulated by said compound.

24. (original) A process for obtaining a compound which modulates apoptosis through the human IDH polypeptide comprising:

(a) measuring the binding of the human IDH polypeptide, or a fragment thereof having viability activity, to a species to which the human IDH polypeptide interacts specifically *in vivo* to produce an anti-apoptotic effect;

(b) contacting said polypeptide or fragment with said compound; and

(c) determining whether the activity of said polypeptide or fragment is affected by said compound.

25. (New) The method according to claim 1, wherein the inhibitor is an siRNA for the IDH gene.

26. (New) The method according to claim 7, wherein the inhibitor is an siRNA for the IDH gene.

Remarks

Claims 1-24 are pending in the subject application. By this amendment, applicants have added new claims 25 and 26, which depend from claims 1 and 7, respectively. Support for new claims 25 and 26 may be found in the specification *inter alia* on page 13, line 29,

page 4, lines 17-28 and page 7, line 34.

Hereinabove, applicants have also amended the specification by replacing Figure 4 with new Figure 4, attached hereto as **Exhibit A.** New figure 4 is submitted to correct an obvious typographical error in which "T" is erroneously recited in place of "U" in an siRNA sequence. This amendment is supported throughout the specification. See, for example, the figure legend for Figure 4.

In addition, applicants have made a corresponding amendment to the Sequence Listing previously submitted which corresponds to Figure 4, i.e. Sequence ID NO: 6, and have submitted a corrected paper copy of the Sequence Listing, attached hereto as **Exhibit B**, a new CRF of the Sequence Listing and a Certification that the Sequence Listing on the new CRF corresponds to the paper copy of the Sequence Listing, attached hereto as **Exhibit C**.

No issue of new matter is raised by this Amendment. Accordingly, applicants respectfully request entry of this Amendment.

Restriction Requirement:

In the April 3, 2006 Office Action, the Examiner required restriction under 35 U.S.C. §121 to one of the following six groups of claims:

I. Claims 12 and 13, drawn to an antisense oligonucleotide capable of inhibiting the expression of the IDH polypeptide;

II. Claims 1-11, drawn to a method for treatment of an apoptosis related disease in a subject comprising

administering to said subject a therapeutically effective amount of an inhibitor of the IDH polypeptide;

III. Claims 14, 16 and 18, drawn to a process for determining the level of the IDH polypeptide in a subject to determine the potential and actual response to chemotherapeutic treatment and the diagnosis of cancer;

IV. Claims 15, 17 and 19, drawn to a process for determining the level of the IDH mRNA in a subject to determine the potential and actual response to chemotherapeutic treatment and the diagnosis of cancer;

V. Claims 20-22, drawn to process for obtaining a compound which modulates apoptosis; and

VI. Claims 23 and 24, drawn to a process for obtaining a compound, which modulates apoptosis through the human IDH polypeptide.

In response, applicants hereby elect, with traverse, the invention identified by the Examiner as Group II, i.e. claims 1-11, drawn to a method for treatment of an apoptosis related disease in a subject comprising administering to said subject a therapeutically effective amount of an inhibitor of the IDH polypeptide.

Species Election for Group II

On pages 6-7 of the April 3, 2006 Office Action, the Examiner further alleged that claims 3-5 and 8-10 are generic to the following thirteen (13) disclosed patentably distinct species of IDH inhibitors:

1. antibody (claims 3 and 8)

2. 2-(4-bromo-2,3-dioxobutylthio)-1 (claims 4 and 9)

3. N6-ethenoadenosine 2',5'-bisphosphate (claims 4 and 9)

4. NADP oxoglutatrate (claims 4 and 9)'

5. o-(carboxymethyl) oxalohydroxamate (claims 4 and 9)

6. oxalylglycine (claims 4 and 9)

7. 3-bromo-2-ketoglutarate (claims 4 and 9)

8. beta-mercapto-alpha-ketoglutarate (claims 4 and 9)

9. beta-methylmercapto-alpha-ketoglutarate (claims 4 and 9)

10. beta-methylmercapto-alpha-hydroxyglutarate (claims 4 and 9)

11. adriamycin (claims 4 and 9)

12. alpha-methylisocitrate (claims 4 and 9)

13. AS fragment comprising consecutive nucleotides having the sequence set forth in SEQ ID NO: 5 (claims 5 and 10)

Further, the Examiner alleged that the products of the above species represent separate and distinct molecules with different structures and functions such that one species could not be interchanged with the other. As such, each species would require different searches and the consideration of different patentability issues. The applicants are therefore required to elect a single disclosed species.

In response, applicants elect, with traverse, the species of siRNA, which is treated in new Claims 25 and 26. The invention of original claims 1-11, and new claims 25 and 26 are now drawn to a method for treatment of an apoptosis related disease in a subject comprising administering to said subject a therapeutically effective amount of an inhibitor of an IDH polypeptide that is an siRNA. Although the elected species, siRNA, as noted above, was not listed by the Examiner, support for applicants' election of siRNA can be found in the specification *inter alia* on page 4, lines 17-28, page 7, line 34 and page 13, line 29.

Applicants respectfully request that the Examiner reconsider and withdraw the restriction requirement in view of the election of Group II, claims 1-11, and the addition of claims 25 and 26. Under 35 U.S.C. §121, restriction may be required if two or more independent and distinct inventions are claimed in one application.

Under M.P.E.P. §802.01, "independent" means there is no disclosed relationship between the subjects disclosed. The invention of group II is drawn to a method for treatment of an apoptosis related disease in a subject comprising administering to said subject a therapeutically effective amount of an inhibitor of the IDH polypeptide. Claims 25 and 26 are drawn to a species for treatment of an apoptosis related disease in a subject comprising administering to said subject a therapeutically effective amount of an inhibitor of the IDH polypeptide which is an siRNA. Applicants therefore maintain that the claims of elected Group II are not independent from the claims of added claims 25 and 26.

Furthermore, under MPEP §803, there are two criteria for a proper

restriction requirement: 1) the invention must be independent or distinct (discussed above), and 2) there must be a serious burden on the Examiner if restriction is required. MPEP §803 unambiguously provides that "[i]f the search and examination of an entire application can be made without serious burden, the examiner must examine it on the merits, even though it includes claims to independent and distinct inventions." Applicants respectfully submit that there would not be a serious burden on the Examiner if restriction is not required between the claims of group II and added claims 25 and 26. A search for prior art material to the patentability of claims 1-11, drawn to a method for treatment of an apoptosis related disease in a subject comprising administering to said subject a therapeutically effective amount of an inhibitor of the IDH polypeptide would necessarily turn up prior art material to the patentability of claims 25 and 26. Any search for treating an apoptosis related disease in a subject comprising administering to said subject a therapeutically effective amount of an inhibitor of the IDH polypeptide will turn up siRNA as an inhibitor of the IDH polypeptide. Since there is no burden on the Examiner to examine the elected Group II, claims 1-11, and elected species siRNA, including new claims 25 and 26 together in the subject application, it is therefore submitted that claims 1-11 and 25 and 26 should be examined on the merits.

If a telephone interview would be of assistance in advancing prosecution of the subject application, applicant's undersigned attorney invites the Examiner to telephone him at the number provided below.

No fee, other than the enclosed fee of $1,080.00 fee for a five-month extension of time, is deemed necessary in connection with the

filing of this amendment. If any additional fee is required, authorization is hereby given to charge the amount of any such fee to Deposit Account No. 03-3125.

Respectfully submitted,

I hereby certify that this correspondence is being deposited this date with the U.S. Postal Service with sufficient postage as first class mail in an envelope addressed to: Mail Stop Amendment, Commissioner For Patents, P.O. Box 1450, Alexandria, VA 22313-1450

10/3/06

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Date

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